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CLINICAL PERSPECTIVES

Should patients with haemorrhage be kept warm?

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It has been more than 95 years since Ernest Starling provided experimental evidence to support the concept that energy of contraction is proportional to the initial length of the cardiac muscle fibre (Patterson & Starling, 1914). This concept, known as Starling's law of the heart, defined the fundamental relationship between cardiac preload (end-diastolic volume or filling pressure) and stroke volume (cardiac performance). Subsequent investigations have revealed that this mechanism can be represented by an 'operational point' that shifts across a family of hyperbolic curves depending on varying physiological conditions. An operational point that functions on the flat portion of the curve is viewed as 'protective' of cardiac performance since a given drop in filling volume or pressure has little impact on stroke volume while function on the steep portion of the curve can lead to drastic reductions in cardiac output with only small decreases in venous return. The latter condition can lead to marked hypotension with subsequent failure to adequately perfuse vital organs.

A reduction in central blood volume (central hypovolaemia) such as that caused by an orthostatic challenge or haemorrhage is one condition that elicits a left and upward shift of the Starling relationship by way of a compensatory sympathetic excitation (Braunwald *et al.* 1967). The resultant increase in myocardial contractility maintains stroke volume in the face of lowered cardiac filling, but the setting of the operational point on a steeper curve places the cardiovascular system at risk for collapse with any further reduction in filling pressure. The latter condition forms the basis for the development of fainting or haemorrhagic shock.

In this issue of *The Journal of Physiology*, Bundgaard-Nielsen and co-workers (2010) studied the impact of central hypovolaemia on Starling's law of the heart by exposing human subjects to lower body negative pressure (LBNP) as a way to progressively reduce central blood volume in three conditions of thermal stress and volume loading. It is not surprising that the reduction in filling pressure (central venous and pulmonary capillary wedge) induced by LBNP resulted in a lower stroke volume. The addition of heat stress (increased body temperature) caused a shift of the entire Starling relationship to a steeper curve. Stroke volume was maintained during thermal stress despite a lowered filling pressure, probably due to a hyperadrenergic effect on myocardial contractility. As a consequence, however, a smaller drop in filling pressure (CVP or PCWP) was required to produce an equal reduction in stroke volume because of movement of the operational point to a steeper Starling curve.

If the reduction in central blood volume were the primary cause for the shift in the Starling relationship, one might expect that volume loading would have returned the operational point to the original curve. Against this expectation, volume loading moved the operational point to the flatter portion of the steeper thermal stress curve. This observation provides new insight into the manner in which alterations in the Starling relationship may be impacted by changes in central blood volume by suggesting that resetting of the operational point to a steeper curve is driven by some stimulus related specifically to heating of the body independent of alterations in central blood volume. Although volume loading added protection against large reductions in stroke volume with drops in filling pressure, continued bleeding with body heating, even during volume loading, could return the operational point to the steeper portion of the curve and subsequently compromise haemodynamic stability.

The findings of the study conducted by Bundgaard-Nielsen and co-workers may have important clinical implications by challenging the practice in emergency medicine of warming patients with haemorrhage. The practice of warming patients with bleeding trauma addresses the contribution of hypothermia to coagulopathy. However, it is unclear which makes the greater contribution to poor outcomes, hypothermia-associated coagulopathy, or the reduction in cell metabolism because of significant blood loss leading to inadequate tissue perfusion (Henderson *et al.* 1999). Ultimately, the problem is haemorrhagic shock which results from inadequate tissue perfusion of vital organs such as the heart and brain. In light of the findings by Bundgaard-Nielsen *et al.*, warming patients could increase the risk of reducing systemic blood flow and tissue perfusion, particularly in the absence of adequate fluid resuscitation, placing the patient at greater risk for promoting cardiovascular collapse and the onset of circulatory shock. Thus, maintaining a 'warm' patient who is bleeding may be a double-edged sword, with haemodynamic consequences that can ultimately compromise benefits to coagulation. In light of evidence that hypothermia can be associated with improved survival (Kheirbek *et al.* 2009), future experiments should be designed to examine the effect of body cooling on the Starling relationship. These may provide the basis for re-evaluation of current practices that emphasize the warming of patients with bleeding trauma. At a minimum, it appears that particular vigilance to volume status should be mandated in re-warming protocols.

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